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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,379	05/30/2001	Donald L. Durden	1857-P02575US1	7235

110 7590 01/15/2003

DANN DORFMAN HERRELL & SKILLMAN
SUITE 720
1601 MARKET STREET
PHILADELPHIA, PA 19103-2307

EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/15/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/870,379	DURDEN, DONALD L.	
	Examin r	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-88* is/are pending in the application.

4a) Of the above claim(s) *1-79 and 83-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group XXVI drawn to in vivo method of inhibiting aberrant angiogenesis using PI3 inhibitor in Paper No. 7 is acknowledged. The traversal is on the ground(s) that several inventions are related as an assay for identification of modulators of PTEN activity and that the inventions have not been shown to be independent and distinct and the examination of all groups would not impose a serious burden on the examiner. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in Paper No. 6. As to the question of burden of search, classification of subject matter in US Patent shoes is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. This examiner notes that claim 83 has been included in two groups i.e., groups XXVI and XXVII in the previous Office Action (Restrictions). Applicant further argues that restriction between several groups is improper because the paired groups are related in that they comprise product-by-process claims. However, a product identified by a screening assay is not a product-by-process, because the screening assay does not describe the process used to make the product. Furthermore, any chemical identified by the claimed screening assay could be identified by a substantially different screening assay, for example one involving ~~frouwth~~ growth or suppression of growth of cancerous cells. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-79, and 84-88 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 80-82 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 80-82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. Claims 80-83 are interpreted as drawn to a method of inhibiting aberrant angiogenesis in vivo by administering a genus of PI3 kinase inhibitors. The specification provides evidence for only two PI3 kinase inhibitors, LY294002 and wortmannin. Based on these two PI3 kinase inhibitors, one cannot predict the types of additional two PI3 kinase inhibitors. Since the genus includes a large number of unpredictable species, possession of only two species is not seen as sufficient to reasonably convey possession of the entire genus. It is concluded that applicants adequately describes LY294002 and wortmannin.

Claims 82 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession** of the claimed invention. Claims 82 is interpreted as drawn to a method of inhibiting aberrant angiogenesis in vivo by administering a genus of AKT inhibitors. The specification teaches neither the molecular structure of any Akt inhibitor nor how to make an AKT inhibitor. It is concluded that applicants does not adequately describe an AKT inhibitor.

Claim 82 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to **enable** one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is interpreted as a method of inhibiting cancer-induced aberrant angiogenesis by administering two active ingredients, namely a PI3

inhibitor and an AKT inhibitor. This rejection has several aspects. The specification fails to provide enblement for the claim drawn to method of using PI3 inhibior and further comprising an AKT inhibitor because the specification does not teach how to make even an AKT inhibitor that could be used in the claimed invention, let alone a broad range of AKT inhibitors. The entire specification talks about treating cancer by inhibiting aberrant angiogenesis (see page 74 Example IV) and it is well known that the art of anticancer drug discovery for cancer therapy by any mechanism including inhibiting aberrant angiogeneis is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed peptide would be useful for treating cancer. In addition, Hartwell et al (Science, 1997, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill

tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2). In addition, the specification does not teach how to deliver an ATK inhibitor to the proper site of action, which appears to be cytosol according to 2nd para, col 1 at page 1751 of Jiang et al (02-15-2002, PNAS vol. 97, pages 1749-1753). The specification does not teach how to make/use a formulation with a targeting molecule. Also, the target cell must not have an alternate means of survival despite action at the proper site for the drug. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The formulation may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. The specification provides insufficient guidance how to make an ATK inhibitor and other issues raised above, and provides no working examples of how to deliver the product to the target site in vivo, and unpredictability in art as regard to cancer treatment, it is concluded that undue experimentation would be required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 80 and 81 are rejected under 35 U.S.C. 102(a) as being anticipated by Hu et al (March 2000, Clinical Cancer Research, vol. 6, pages 880-886) as evidenced

by Jiang et al (02-15-2002, PNAS vol. 97, pages 1749-1753) and Oikawa et al (1996, European Journal of Pharmacology, vol. 318, pages 93-96).

The claims are drawn to method of inhibiting aberrant angiogenesis caused by cancer comprising administering a PI3 inhibitor.

Hu teaches administering a PI3 inhibitor to tumor-bearing mice.The method of the prior art comprises the same method steps as claimed in the instant invention, that is, administering an inhibitor of a PI3 kinase to in vivo patient with cancer-induced aberrant angiogenesis, thus the claimed method is anticipated because the method will inherently lead to inhibit aberrant angiogenesis on the tumor cells. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Note Jiang et al and Oikawa et al for mechanism of action of PI3 kinase inhibitor.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800

Misook Yu
January 8, 2003